KAISER PERMANENTE®

Kaiser Foundation Health Plan of Washington

Clinical Review Criteria

MRI- Ultrasound fusion for guidance of targeted prostate biopsy

- MRI/TRUS

Criteria

For Medicare Members

Source	Policy
CMS Coverage Manuals	None
National Coverage Determinations (NCD)	None
Local Coverage Determinations (LCD)	None
Local Coverage Article	None
KPWA Medical Policy	Due to the absence of a NCD, LCD, or other coverage guidance, KPWA has chosen to use their own Clinical Review Criteria, "MRI- Ultrasound fusion for guidance of targeted prostate biopsy," for medical necessity determinations. Use the Non-Medicare criteria below.

For Non-Medicare Members

There is insufficient evidence in the published medical literature to show that this service/therapy is as safe as standard services/therapies and/or provides better long-term outcomes than current standard services/therapies.

> The following information was used in the development of this document and is provided as background only. It is provided for historical purposes and does not necessarily reflect the most current published literature. When significant new articles are published that impact treatment option, KPWA will review as needed. This information is not to be used as coverage criteria. Please only refer to the criteria listed above for coverage determinations.

Background

Prostate cancer is the second most leading cause of cancer in men around the globe (Fitzmaurice et al., 2017). In the United States, one in six men has a lifetime risk of prostate cancer (Siegel, Ward, Brawley, & Jemal, 2011). Prostate cancer screening is subject to controversy; major guidelines highlight the importance of informed decision-making; but despite the controversy, prostate specific antigen (PSA) and or digital rectal examination (DRE) can be performed. With increased level of PSA and/or abnormal features on DRE, prostate biopsy guided by ultrasound is indicated. There are different approaches in performing prostate biopsy; these include transrectal and transperineal methods; however the most widely utilized is the transrectal ultrasound approach (Heidenreich et al., 2011). Prostate biopsy is associated with urinary tract infections (UTI), sepsis, and Fournier gangrene (Puig et al., 2006). Other complications include hematuria, and hematospermia. Other modalities have been developed and the magnetic resonance (MR)-targeted biopsy, especially the MRI/ultrasound fusion-guided has been the center of attention.

Back to Top

The MRI/ultrasound fusion-guided biopsy allows the visualization of the prostate through different angles and combines MRI images with transrectal ultrasound (TRUS) images while ultrasound probe is still inserted in the patient. The goal is to accurately identify suspicious areas in the prostate. First, MRI is performed and MRI images are obtained. Next, TRUS is performed and while this procedure is being done, images are also captured. Then, these images are inserted in the computer with special software to match the images (registration). This provides 3D, fused images that guide the insertion of the biopsy needle to suspicious areas (from http://sperlingprostatecenter.com/mri-guided-biopsy-vs-fusion/).

Three imaging series are obtained during the MRI. These consist of T2-weighted (T2W) imaging, diffusion weighted imaging (DWI) with apparent diffusion coefficient (ADC), and dynamic contrast-enhanced (DCE) imaging (Hegde et al., 2013). The T2W imaging assesses local tissue water and delimits the transition and peripheral zones. The DWI assesses the mobility of water molecules and the ADC is a measure of this motion. The DCE imaging explores vascularity.

Medical Technology Assessment Committee (MTAC)

Date: 10/18/2017 MTAC REVIEW

MRI–ultrasound fusion for guidance of targeted prostate biopsy

Evidence Conclusion:

One study reported findings related to reproducibility and the rest of the studies assessed clinical validity. The study reporting on reproducibility also assessed clinical validity. Studies evaluating clinical utility were not identified.

Reproducibility: The study (Rastinehad et al., 2016) reporting on reproducibility validated MRI-Fusion guided biopsy in an external, independent cohort and concluded that MRI/Fusion guided biopsy may be reproducible (See Evidence Table 2) **Clinical validity** (See Evidence Tables 1 & 2) Six studies were reviewed; one was a meta-analysis (Jiang et al., 2016); four were prospective cohort study (Gordetsky, Thomas, Nix, & Rais-Bahrami, 2017; Hansen et al., 2017; Kongnyuy et al., 2017; Zhang et al., 2017) and one was a randomized controlled trial (Arsov et al., 2015). Studies were conducted on biopsy-naïve patients as well as patients with previous negative prostate biopsy. The main comparator was TRUS biopsy. Patient's characteristics included: age which varied from 37 to 87 years, PSA ranged from 0.3 to104, and prostate volume varied from 12-220. The sampling method was transrectal for the most part, and the number of cores per lesion ranged from 1-24; the definition of clinically significant prostate cancer varied. In patients with first prostate biopsy (at risk of prostate cancer) and in patients with MRI suspected cancer, the detection rates of clinically significant prostate cancer as well as overall prostate cancer were conflicting. In the meta-analysis, findings favored MRI-Fusion targeted biopsy; in the studies subsequent to the meta-analysis no significant difference was reported between MRI-Fusion targeted biopsy and standard TRUS biopsy. Complications were not assessed in the majority of studies reviewed. However, one study (Arsov et al., 2015) reported febrile prostatitis. Limitations included the following: non-randomized nature of studies, publication bias and heterogeneity in the meta-analysis, variability in the definition of clinically significant cancer, method of targeted bx, number of cores per target, bias inherent to observational study, and inconsistencies in the direction of findings. For these reasons, the level of evidence was deemed low. **Clinical utility:** Studies evaluating the impact of MRI-Fusion targeted biopsy on health outcomes were not identified. **Other studies:** A systematic review (Gayet et al., 2016) reported no difference between MRI/Fusion platforms in prostate cancer detection. However, MRI/US fusion – guided targeted biopsy may detect more clinically significant prostate cancers.

Conclusion:

- Six studies were reviewed; the studies were prospective cohort study in design and assessed overall prostate cancer detection rate as well as clinically significant detection rates.
- Only one study evaluated safety
- The direction of findings was not consistent
- Low evidence shows that MRI-US Fusion may be more accurate than TRUS biopsy in biopsy naïve patients and in patients with previous negative biopsy.

The use of MRI–ultrasound fusion for guidance of targeted prostate biopsy does not meet the *Kaiser Permanente Medical Technology Assessment Criteria.*

 Back to Top

Date: 07/09/2018 MTAC REVIEW

MRI–TRUS fusion targeted prostate biopsy post negative biopsy

Evidence Conclusion:

Clinical validity

Three studies from the previous review that assessed patients with negative prostate biopsy reported inconsistent results. One meta-analysis showed that MRI-US fusion prostate biopsy may detect more overall prostate cancer and clinically significant prostate cancer than TRUS biopsy (Jiang et al., 2016). One observational study (Hansen et al., 2017) reported no statistically significant difference between MRI-US fusion prostate biopsy and TRUS biopsy in detecting clinically significant prostate cancer among patients with previous negative biopsy and PI-RAD 4-5 (the detection rate was higher for MRI-US fusion and statistically significant with PI-RAD 5). One RCT (Arsov et al., 2015) reported no significant difference in overall prostate cancer and significant prostate cancer detection rates between MRI-TRUS fusion guided biopsy and TRUS biopsy.

Nine studies (Evidence table 1) are reviewed in the current report. Two are meta-analyses of observational study and seven are cohort study.

Meta-analyses

The meta-analyses included 12 and 16 studies (3,225 men and 1926 men). Both meta-analyses included men with rising PSA (≥4ng/L) and/or abnormal digital rectal exam (DRE). Multiparametric MRI was performed before fusion and patients with suspicious lesions underwent fusion biopsy. MRI-US fusion biopsy and TRUS biopsy were performed in the same session. History of prior biopsy was mixed but the outcomes reported focused on patients with previous negative biopsy. Four studies included patients with negative biopsy in one meta-analysis (Schoots et al., 2015) and 3 in the second meta-analysis (Tang et al., 2018). Age ranged from 40 to 80 years, PSA varied from 0.2 to 100, prostate volume ranged from 8-200.

Overall prostate cancer (PCa): Inconsistent findings were reported. No statistically significant difference was reported between MRI-US fusion biopsy and TRUS biopsy in one meta-analysis (Tang et al., 2018) (OR, 1.33 (0.99 – 1.77); I2 0%; p=0.06). MRI-US fusion biopsy significantly detected more PCa than TRUS biopsy (Relative sensitivity 1.62 (1.02, 2.57), p=0.001) (Schoots et al., 2015).

Significant prostate cancer: Both meta-analyses reported that MRI-US fusion biopsy detected more significant PCa than TRUS biopsy but the significance differed [(OR, 1.89 (1.32, 2.72); I2 0%; p=0.0006) (Tang et al., 2018) Relative sensitivity 1.54 (1.05, 2.26), p=0.64 (Schoots et al., 2015)].

Insignificant prostate cancer: TRUS biopsy significantly detected more insignificant PCa than fusion biopsy [32% (2 – 91%) vs 68% (9 – 98%)].

Both meta-analyses met 7 and 8 criteria of AMSTAR; however, the overall quality was low to fair.

Observational study

Patients included were men with elevated PSA levels or abnormal digital rectal exam with prior negative biopsies and suspicious lesions on multiparametric MRI. The number of patients ranged from 105 to 1003. Mean age varied from 62 to 68 years; mean PSA ranged from 7.5 to 13.9 ng/mL; mean prostate volume varied from 50 to 64.6 cm 3. All patients underwent multiparametric MRI (mpMRI) and those with suspicious lesions underwent fusion biopsy and TRUS biopsy.

Definition of clinically significant prostate cancer varied across studies. Classification of lesions on mpMRI varied across studies as well as the number of biopsy cores. MRI-US fusion platforms also varied.

Prostate cancer detection rate: Conflicting results were reported. The detection rates of PCa was higher in patients undergoing TRUS biopsy than fusion biopsy in three studies (Cash, Maxeiner, et al., 2016; Sonn et al. 2014; Brock et al., 2015). However, the significance of the findings was unknown.

Two studies (Maxeiner et al., 2015; Salami et al., 2015) reported higher PCa detection rate for MRI-US fusion biopsy but the result was not significant in one of the studies [52.1% (73/140) and 48.6% (68/140), (P = 0.435)]. One study (Radtke et al., 2015) reported no significant difference between the two procedures.

Clinically significant prostate cancer (CSPCa): The detection rate of CSPCa was higher in patients undergoing fusion biopsy than TRUS biopsy across the studies except in one study (Cash, Maxeiner, et al., 2016) that reported similar detection rate. However, the significance of the findings was not known. Only one study (Salami et al., 2015) reported the significance of the findings and reported statistically significant detection of CSPCa for MRI-US fusion biopsy over TRUS biopsy (47.9% vs 30.7%; P < 0.001). Nevertheless, one study (Radtke et al., 2015) reported no significant difference between the two procedures.

Quality of body of evidence: The risk of bias of these cohort studies was assessed using Cochrane risk of bias tool. Overall, the risk of bias was high. In addition, there were inconsistency issues, but no indirectness issues. The quality of the body of evidence from the observational studies was low.

Clinical utility

Search was performed irrespective of patients with prior negative biopsy history. Studies evaluating direct clinical impact on patients were lacking.

Safety – complications

 Back to Top

Search was performed irrespective of patients with prior negative biopsy history. Four studies were assessed.
A randomized controlled trial (Arsov et al., 2015) comparing MRI guided in-bore biopsy (Grp A) versus MRI-TRUS fusion-guided biopsy (Grp B) reported 2 (1.9%) febrile prostatitis requiring hospitalization and IV antibiotics in Grp A and 1 (1%) in Grp B. No other adverse events requiring admission occurred.
A cohort study (Huang et al., 2016) including 242 patients (144 underwent TRUS, 98 underwent MRI-TRUS fusion biopsy) reported no significant difference in terms of major complications such as sepsis, bleeding and other complications that necessitated admission.
A prospective cohort study (Kuru et al., 2013) of 347 men reported that the most common adverse events were hematuria [152 (51%)], brief reduction in erectile dysfunction [79 (26.3%)] but no permanent erectile dysfunction, and perineal hematoma [43 (14%)]. These adverse events were not attributable to a specific type of biopsy since both fusion and systematic biopsy were performed during same session.
A retrospective study (Borkowetz et al., 2015) of 263 patients reported: hematuria with evacuation of bladder was 0.7%, infection treated with IV antibiotics was 3%, short-term catheterization due to urinary retention was 7%. However, these complications could not be attributed to a specific type of biopsy because fusion biopsy and TRUS biopsy were performed during the same session.

Conclusion

- In patients with clinical suspicion of prostate cancer and previous negative biopsy with at least one suspicious lesion on multiparametric MRI,
    - Low evidence shows inconsistencies in prostate cancer detection rate between MRI-US fusion biopsy and TRUS biopsy.
    - Low evidence indicates that MRI-US fusion biopsy may have higher detection rate of clinically significant prostate cancer than TRUS biopsy.
- Adverse events: Four studies were reviewed. No significant difference was reported in two studies that could attribute type of biopsy to adverse events. However, adverse events could not be attributed to the type of biopsy in the rest of the studies.

The use of MRI-TRUS fusion targeted prostate biopsy post negative biopsy doesn't meet the *Kaiser Permanente Medical Technology Assessment Criteria.*

Date Created	Date Reviewed	Date Last Revised
02/06/2018	02/06/2018[MPC],	08/07/2018

[MPC] Medical Policy Committee

Revision History	Description
08/07/2018	Added MTAC review from 7/9/18 for fusion prostate biopsy post negative biopsy

Codes

No specific codes

Back to Top